

RMD-130  
CENTRAL CENTER

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**Section I (Amendments to the Claims)**

Please amend claims 1, 6, 10, 13, 14, and 17-20 and add new claims 23-43, as in the following listing of claims 1-43:

1. (Currently amended) An apparatus for sequentially separating components of milk, comprising:
  - (a) a milk source;
  - (b) one or more cross-flow filtration modules communicatively connected to said milk source, for generating one or more filtration fractions;
  - (c) one or more fluid delivery means conduit connected to each of said cross-flow filtration modules to effectuate flow of milk through said cross-flow filtration modules for separation of milk components; and
  - (d) one or more means fluid collection conduit downstream of each of said cross-flow filtration modules for sequentially capturing one or more filtration fractions generated by the cross-flow filtration modules.
2. (Original) An apparatus according to claim 1, wherein each cross-flow filtration module comprises at least one permeate, at least one inlet, at least one outlet, and multiple fluid-flow sub-channels that are of equal length between the inlet and the outlet.
3. (Original) An apparatus according to claim 1, wherein the one or more cross-flow filtration modules comprise a filtration membrane selected from the group consisting of cellulose-based membranes, polymer-based membranes, and ceramic-based membranes.
4. (Original) An apparatus according to claim 1, further comprising a cream separator upstream of said cross-flow filtration modules for removing at least a portion of fatty component from the milk.

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5. (Original) An apparatus according to claim 1, further comprising a pasteurizer upstream and/or downstream of said one or more cross-flow filtration modules for pasteurizing the milk.
6. (Currently amended) An apparatus according to claim 1, further comprising temperature ~~controlling/monitoring means~~ controller or monitor for controlling and monitoring temperature of said milk and/or filtration fractions generated by the one or more cross-flow filtration modules.
7. (Original) An apparatus according to claim 1, comprising a cross-flow filtration module for separating the milk from the milk source into a casein-rich fraction and a casein-depleted fraction.
8. (Original) An apparatus according to claim 7, wherein the cross-flow filtration module comprises membranes selected from the group consisting of cellulose-based membranes, polymer-based membranes, and ceramic-based membranes.
9. (Original) An apparatus according to claim 7, wherein the cross-flow filtration module comprises a membrane having an average pore size in a range of from about 100KD to about 3000KD.
10. (Currently amended) An apparatus according to claim 7, wherein the cross-flow filtration module comprises a membrane having an average pore size in a range of from about 100KD to about 1000KD, ~~selected from the group consisting of cellulose-based membranes selected from the group consisting of cellulose membranes, cellulose acetate membranes, and regenerated cellulose membranes.~~
11. (Original) An apparatus according to claim 7, wherein the cross-flow filtration module comprises a polymeric membrane having an average pore size between 800KD and 2500KD and/or a measured bubble point between 65 and 120 PSIG.
12. (Original) An apparatus according to claim 7, wherein the cross-flow filtration module comprises a regenerated cellulose membrane having an average pore size of about 100KD.

13. (Currently amended) An apparatus according to claim 1, comprising:

an optional first cross-flow filtration module downstream of the milk source and communicatively connected thereto for filtering out all or at least a portion of bacteria contained in the milk;

a second cross-flow filtration module, downstream of the first cross-flow filtration module if provided and communicatively connected thereto, or if not provided, then communicatively connected directly to the milk source, which separates the milk into a casein-rich fraction and a casein-depleted fraction;

means a first fluid collection conduit connected to said second cross-flow filtration module for capturing the casein-rich fraction;

a third cross-flow filtration module downstream of the second cross-flow filtration module and communicatively connected thereto, which receives the casein-depleted fraction and further separates it into a fraction that is enriched with albumin and immunoglobulins and a fraction that is depleted of albumin and immunoglobulins;

means a second fluid collection conduit connected to said third cross-flow filtration module for capturing the fraction that is enriched with albumin and immunoglobulins;

a fourth cross-flow filtration module downstream of the third cross-flow filtration module and communicatively connected thereto, which receives the fraction that is depleted of albumin and immunoglobulins and further separates it into a  $\beta$ -lactoglobulin-rich fraction and a  $\beta$ -lactoglobulin-depleted fraction;

means a third fluid collection conduit connected to said fourth cross-flow filtration module for capturing the  $\beta$ -lactoglobulin-rich fraction;

a fifth cross-flow filtration module downstream of the fourth cross-flow filtration module and communicatively connected thereto, which receives the  $\beta$ -lactoglobulin-depleted fraction and further separates it into a  $\alpha$ -lactalbumin-rich fraction and a  $\alpha$ -lactalbumin-depleted fraction;

means a fourth fluid collection conduit connected to said fifth cross-flow filtration module for capturing the  $\alpha$ -lactalbumin-rich fraction;

a sixth cross-flow filtration module downstream of the fifth cross-flow filtration module and communicatively connected thereto, which receives the  $\alpha$ -lactalbumin-depleted fraction and further separates it into a complex carbohydrates rich fraction and a complex carbohydrates depleted fraction;

means a fifth fluid collection conduit connected to said sixth cross-flow filtration module for capturing the complex carbohydrates rich fraction;

a seventh cross-flow filtration module downstream of the sixth cross-flow filtration module and communicatively connected thereto, which receives the complex carbohydrates depleted fraction and further separates it into a lactose-rich fraction and a lactose-depleted fraction; and

means a sixth fluid collection conduit connected to said seventh cross-flow filtration module for capturing the lactose-rich fraction;

means a discharge conduit for discharging and/or recycling the lactose-depleted fraction.

14. (Currently amended) An apparatus according to claim 1, comprising:

an optional first cross-flow filtration module downstream of the milk source and communicatively connected thereto for filtering out all or at least a portion of bacteria contained in the milk;

a ~~first~~ second cross-flow filtration module downstream of said first cross-flow filtration module or the milk source and communicatively connected ~~thereto~~ to said first cross-flow filtration or the milk source, which separates the milk into a casein-rich fraction and a casein-depleted fraction;

means a first fluid collection conduit connected to said ~~first~~ second cross-flow filtration module for capturing the casein-rich fraction;

~~a second cross-flow filtration module downstream of the first cross-flow filtration module and communicatively connected thereto, which receives the casein-depleted fraction and further separates it into a fraction that is enriched with albumin and immunoglobulins and a fraction that is depleted of albumin and immunoglobulins;~~

~~means connected to said second cross-flow filtration module for capturing the fraction that is enriched with albumin and immunoglobulins;~~

a third cross-flow filtration module downstream of the second cross-flow filtration module and communicatively connected thereto, which receives the casein-depleted fraction that is ~~depleted of albumin and immunoglobulins~~ and further separates it into a  $\beta$ -lactoglobulin-rich fraction and a  $\beta$ -lactoglobulin-depleted fraction;

means a second fluid collection conduit connected to said third cross-flow filtration module for capturing the  $\beta$ -lactoglobulin-rich fraction;

a fourth cross-flow filtration module downstream of the third cross-flow filtration module and communicatively connected thereto, which receives the  $\beta$ -lactoglobulin-depleted fraction and further separates it into a  $\alpha$ -lactalbumin-rich fraction and a  $\alpha$ -lactalbumin-depleted fraction;

~~means~~ a third fluid collection conduit connected to said fourth cross-flow filtration module for capturing the  $\alpha$ -lactalbumin-rich fraction;

~~a fifth cross-flow filtration module downstream of the fourth cross-flow filtration module and communicatively connected thereto, which receives the  $\alpha$ -lactalbumin-depleted fraction and further separates it into a complex carbohydrates rich fraction and a complex carbohydrates depleted fraction;~~

~~means connected to said fifth cross-flow filtration module for capturing the complex carbohydrates rich fraction;~~

~~a sixth cross flow filtration module downstream of the fifth cross flow filtration module and communicatively connected thereto, which receives the complex carbohydrates depleted fraction and further separates it into a lactose rich fraction and a lactose depleted fraction; and~~

~~means a fourth fluid collection conduit connected to said sixth fourth cross-flow filtration module for capturing the lactose rich  $\alpha$ -lactalbumin-depleted fraction for subsequent processing selected from the group consisting of cross-flow filtration, lactose recovery, discharging, recycling, capturing, further processing and recycling;~~

~~means for discharging and/or recycling the lactose depleted fraction.~~

15. (Original) An apparatus according to claim 13, further comprising a pasteurizer upstream and/or downstream of any of the cross-flow filtration modules for pasteurizing the milk source or any one or more filtration fractions generated by the cross-flow filtration modules.
16. (Original) An apparatus according to claim 14, further comprising a pasteurizer upstream and/or downstream of any of the cross-flow filtration modules for pasteurizing the milk source or any one or more filtration fractions generated by the cross-flow filtration modules.
17. (Currently amended) An apparatus according to claim 13, comprising multiple fluid delivery ~~means conduits~~ arranged in a manner that each cross-flow filtration module is connected to at least one fluid delivery ~~means conduit~~, said fluid delivery ~~means conduits~~ functioning to effectuate a flow of the milk or a fraction of the milk through each cross-flow filtration module.
18. (Currently amended) An apparatus according to claim 14, comprising multiple fluid delivery ~~means conduits~~ arranged in a manner that each cross-flow filtration module is connected to at least one fluid delivery ~~means conduit~~, said fluid delivery ~~means conduits~~ functioning to effectuate a flow of the milk or a fraction of the milk through each cross-flow filtration module.

19. (Currently amended) An apparatus according to claim 16, further comprising temperature ~~controlling/monitoring means~~ controller or monitor for controlling and monitoring temperature of said milk and/or filtration fractions generated by the cross-flow filtration modules.
20. (Currently amended) An apparatus according to claim 17, further comprising temperature ~~controlling/monitoring means~~ controller or monitor for controlling and monitoring temperature of said milk and/or filtration fractions generated by the cross-flow filtration modules.
21. (Original) An apparatus according to claim 16, further comprising a cream separator upstream of said cross-flow filtration modules for removing all or at least a portion of fatty component from the milk.
22. (Original) An apparatus according to claim 17, further comprising a cream separator upstream of said cross-flow filtration modules for removing all or at least a portion of fatty component from the milk.
23. (New) An apparatus according to claim 1, comprising:

an optional first cross-flow filtration module downstream of the milk source and communicatively connected thereto for filtering out all or at least a portion of bacteria contained in the milk;

a second cross-flow filtration module, downstream of the first cross-flow filtration module if provided and communicatively connected thereto, or if not provided, then communicatively connected directly to the milk source, which separates the milk into a casein-rich fraction and a casein-depleted fraction;

a first fluid collection conduit connected to said second cross-flow filtration module for capturing the casein-rich fraction;

a third cross-flow filtration module downstream of the second cross-flow filtration module and communicatively connected thereto, which receives the casein-depleted fraction and further separates it into a fraction that is enriched with albumin and immunoglobulins and a fraction that is depleted of albumin and immunoglobulins;

a second fluid collection conduit connected to said third cross-flow filtration module for capturing the fraction that is enriched with albumin and immunoglobulins;

a fourth cross-flow filtration module downstream of the third cross-flow filtration module and communicatively connected thereto, which receives the fraction that is depleted of albumin and immunoglobulins and further separates it into a  $\beta$ -lactoglobulin-rich fraction and a  $\beta$ -lactoglobulin-depleted fraction;

a third fluid collection conduit connected to said fourth cross-flow filtration module for capturing the  $\beta$ -lactoglobulin-rich fraction;

a fifth cross-flow filtration module downstream of the fourth cross-flow filtration module and communicatively connected thereto, which receives the  $\beta$ -lactoglobulin-depleted fraction and further separates it into a  $\alpha$ -lactalbumin-rich fraction and a  $\alpha$ -lactalbumin-depleted fraction;

a fourth fluid collection conduit connected to said fifth cross-flow filtration module for capturing the  $\alpha$ -lactalbumin-rich fraction;

a fifth fluid collection conduit connected to said fifth cross-flow filtration module for capturing the  $\alpha$ -lactalbumin-depleted fraction for subsequent processing selected from the group consisting of cross-flow filtration, lactose recovery, discharging, recycling, capturing, further processing and recycling.

24. (New) An apparatus according to claim 23, further comprising a pasteurizer upstream and/or downstream of any of the cross-flow filtration modules for pasteurizing the milk source or any one or more filtration fractions generated by the cross-flow filtration modules.

25. (New) An apparatus according to claim 23, comprising multiple fluid delivery conduits arranged in a manner that each cross-flow filtration module is connected to at least one fluid delivery conduit, said fluid delivery conduits functioning to effectuate a flow of the milk or a fraction of the milk through each cross-flow filtration module.
26. (New) An apparatus according to claim 23, further comprising temperature controller or monitor for controlling and monitoring temperature of said milk and/or filtration fractions generated by the cross-flow filtration modules.
27. (New) An apparatus according to claim 23, further comprising a cream separator upstream of said cross-flow filtration modules for removing all or at least a portion of fatty component from the milk.
28. (New) The apparatus of claim 1, wherein the milk source comprises a transgenic or hyper-immunized mammal.
29. (New) A method for isolating therapeutic compound from milk of a transgenic and/or hyper-immunized mammal, comprising the steps of:
  - (a) providing a source of milk from a transgenic and/or hyper-immunized mammal;
  - (b) flowing the milk through a cross-flow filtration module to form a casein-rich retentate fraction and a casein-depleted permeate fraction;
  - (c) capturing the casein-rich retentate fraction;
  - (d) isolating the therapeutic compound from the casein-depleted permeate fraction.
30. (New) The method of claim 29, wherein isolating the therapeutic compound is accomplished by using a technique selected from the group consisting of precipitation, cross-flow filtration, chromatography and cross-flow chromatography.
31. (New) The method of claim 29, wherein said compound is selected from the group consisting of blood clotting factors, proteins, hormones, monoclonal antibodies, and immunoglobulins.
32. (New) The method of claim 29, wherein said compound is useful for treating or preventing a disease selected from the group consisting of gastrointestinal tract disorder, hemophilia,

leukemia, liver disease, diabetes, PKU, viral diseases, bacterial diseases, osteoarthritis, enzymatic deficiencies, protein deficiencies, Alzheimer, infection and cancer.

33. (New) The method of claim 29, further comprising the step of flowing the milk from the milk source through a cream separator to remove all or at least a portion of the fatty component of the milk before flowing said milk through the cross-flow filtration module.
34. (New) The method of claim 29, further comprising the step of pasteurizing the milk using a pasteurizer before flowing said milk through the cross-flow filtration module.
35. (New) The method of claim 29, further comprising the step of flowing the milk through an additional cross-flow filtration module to filter out bacteria before step (b).
36. (New) A method for sequentially fractionating milk, comprising the steps of:
  - (a) providing a source of milk;
  - (b) optionally, flowing the milk through a first cross-flow filtration module to form a casein-rich retentate fraction and a casein-depleted permeate fraction;
  - (c) optionally, capturing the casein-rich retentate fraction;
  - (d) flowing the milk or the casein-depleted permeate fraction through a second cross-flow filtration module to form a protein concentrate fraction and a protein-depleted permeate fraction;
  - (e) capturing or discharging the protein-depleted permeate fraction;
  - (f) flowing the protein concentrate fraction through a third cross-flow filtration module to form a  $\beta$ -lactoglobulin-rich fraction and a  $\beta$ -lactoglobulin-depleted permeate fraction;
  - (g) capturing the  $\beta$ -lactoglobulin-rich fraction;
  - (h) flowing the  $\beta$ -lactoglobulin-depleted fraction through a fourth cross-flow filtration module to form a  $\alpha$ -lactalbumin-rich fraction and a  $\alpha$ -lactalbumin-depleted permeate fraction;
  - (i) capturing the  $\alpha$ -lactalbumin-rich fraction; and
  - (j) capturing or discharging the  $\alpha$ -lactalbumin-depleted permeate fraction.
37. (New) The method of claim 36, further comprising the step of recombining the protein-depleted permeate fraction captured in step (e), the  $\beta$ -lactoglobulin-rich fraction captured

in step (g), and the  $\alpha$ -lactalbumin-depleted permeate fraction captured in step (j) to form a whey protein concentrate.

38. (New) The method of claim 36, further comprising the step of using the  $\alpha$ -lactalbumin-rich fraction captured in step (i) to form infant formula.
39. (New) A system for sequentially fractionating milk, comprising:
- (a) a source of milk;
  - (b) optionally, a first cross-flow filtration module in fluid communication with said source of milk for separating the milk into a casein-rich retentate fraction and a casein-depleted permeate fraction;
  - (c) optionally, a first fluid collection conduit connected to said first cross-flow filtration module for capturing the casein-rich retentate fraction;
  - (d) a second cross-flow filtration module in fluid communication with said source of milk or said first cross-flow filtration module for separating the milk or the casein-depleted permeate fraction into a protein concentrate fraction and a protein-depleted permeate fraction;
  - (e) a second fluid collection conduit connected to said second cross-flow filtration module for capturing or discharging the protein-depleted permeate fraction;
  - (f) a third cross-flow filtration module in fluid communication with said second cross-flow filtration module for separating the protein concentrate fraction into a  $\beta$ -lactoglobulin-rich fraction and a  $\beta$ -lactoglobulin-depleted permeate fraction;
  - (g) a third fluid collection conduit connected to said third cross-flow filtration module for capturing the  $\beta$ -lactoglobulin-rich fraction;
  - (h) a fourth cross-flow filtration module in fluid communication with said third cross-flow filtration module for separating the  $\beta$ -lactoglobulin-depleted fraction into an  $\alpha$ -lactalbumin-rich fraction and an  $\alpha$ -lactalbumin-depleted permeate fraction;
  - (i) a fourth fluid collection conduit connected to said fourth cross-flow filtration module for capturing the  $\alpha$ -lactalbumin-rich fraction; and
  - (j) a fifth fluid collection conduit connected to said fourth cross-flow filtration module for capturing or discharging the  $\alpha$ -lactalbumin-depleted permeate fraction.

40. (New) An infant formula comprising an  $\alpha$ -lactalbumin-rich fraction devoid of any unnatural chemical additives.
41. (New) A nutraceutical product comprising a  $\beta$ -lactoglobulin-rich fraction devoid of any unnatural chemical additives.
42. (New) An infant formula comprising an  $\alpha$ -lactalbumin-rich fraction devoid of chemical precipitants.
43. (New) A nutraceutical product comprising a  $\beta$ -lactoglobulin-rich fraction devoid of chemical precipitants.